Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	58	thrombin near6 ("215" or "217" or "227" or "229")	USPAT	OR	OFF	2006/02/08 19:10
L2	1012	("215" or "227") near6 (tryptophan or trp or W)	USPAT	OR	OFF	2006/02/08 19:12
L3	2	l1 and l2	USPAT	OR	OFF	2006/02/08 19:12

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NEWS 10	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 11	JAN 17	Pre-1988 INPI data added to MARPAT
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=> s thrombin (6A) (215 or 217 or 227 or 229)
L1          37 THROMBIN (6A) (215 OR 217 OR 227 OR 229)

=> s (215 or 227) (6A) (tryptophan or trp or W )
L2         413 (215 OR 227) (6A) (TRYPTOPHAN OR TRP OR W )

=> s l1 and l2
L3           7 L1 AND L2

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L4   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
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AN 2001:549847 CAPLUS
DN 135:270557
TI Mutation of W215 compromises thrombin cleavage of fibrinogen, but not of
PAR1 or protein C
AU Ayala, Youhna M.; Arosio, Daniele; Di Cera, Enrico
CS Department of Biochemistry and Molecular Biophysics, Washington University
School of Medicine, St. Louis, MO, 63110, USA
SO Annals of the New York Academy of Sciences (2001), 936(Fibrinogen), 456-458
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
AB W215 is a highly conserved residue that shapes the S3 and S4 specificity
sites of thrombin. Replacement of W215 with Phe produces modest effects
on thrombin function, whereas the W215Y replacement significantly
compromises the amidolytic activity toward synthetic and natural
substrates. Replacement of W215 with Ala reduces fibrinogen and PAR4
cleavage 500-fold and 280-fold, resp. On the other hand, the mutant
decreases protein C activation and PAR1 cleavage only threefold and
25-fold, resp. The W215A mutant cleaves PAR1 with a specificity constant
more than 13-fold greater than that of fibrinogen and protein C, and
800-fold greater than PAR4. This is the first thrombin derivative to be
described that functions as an almost exclusive activator of PAR1. The
environment of W215 influences differentially three physiol. important
interactions of thrombin, a feature that should assist in the sep. study
of each of these functions in vivo.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 1
AN 2001021359 MEDLINE
DN PubMed ID: 10831587
TI Fluorescence properties and functional roles of **tryptophan** residues 60d, 96, 148, 207, and **215** of **thrombin**.
AU Bell R; Stevens W K; Jia Z; Samis J; Cote H C; MacGillivray R T; Nesheim M
E

CS Department of Biochemistry, Queen's University, Kingston, Ontario K7L 3N6,
Canada.
SO Journal of biological chemistry, (2000 Sep 22) 275 (38) 29513-20.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200011
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001103
AB Conservative Trp-to-Phe mutations were individually created in human thrombin at positions 60d, 96, 148, 207, and 215. Fluorescence intensities for these residues varied by a factor of 6. Residues 60d, 96, 148, and **215** transferred energy to the **thrombin** inhibitor 5-dimethylaminonaphthalene-1-sulfonylarginine-N-(3-ethyl-1,5-pentanediyl)amide efficiently, but residue 207 did not. Intensities correlated inversely with exposure to solvent, and measured and theoretical energy transfer efficiencies agreed well. Function was measured with respect to fibrinogen clotting, platelet and factor V activation, inhibition by antithrombin, and the thrombomodulin-dependent activation of protein C and thrombin-activable fibrinolysis inhibitor (TAFI). All activities of W96F and W207F ranged from 74 to 154% of the wild-type activity. This was also true for W148F, except for inhibition by antithrombin, where it showed 60% activity. W60dF was deficient by 30, 57, and 43% with fibrinogen clotting, platelet activation, and factor V cleavage (Arg(1006)), respectively. W215F was deficient by 90, 55, and 56% with fibrinogen clotting, platelet activation, and factor V cleavage (Arg(1536)). With protein C and TAFI, W96F, W148F, and W207F were normal. W60dF, however, was 76 and 23% of normal levels with protein C and TAFI, respectively. In contrast, W215F was 25 and 124% of normal levels in these reactions. Thus, many activities of thrombin are retained upon

substitution of Trp with Phe at positions 96, 148, and 207. Trp(60d),
however, appears to be very important for TAFI activation, and Trp
(**215**) appears to very important for clotting and protein C activation.

L4 ANSWER 3 OF 4 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 1998:331489 BIOSIS
DN PREV199800331489
TI **Tryptophan 215** of **thrombin** is necessary for efficient fibrinogen clotting activity.
AU Bell, R. [Reprint author]; Boffa, M. B.; Stevens, W.; Cote, H.; Macgillivary, R.; Jia, Z.; Nesheim, M.
CS Queen's Univ., Kingston, ON, Canada
SO FASEB Journal, (April 24, 1998) Vol. 12, No. 8, pp. A1416. print.
Meeting Info.: Meeting of the American Society for Biochemistry and
Molecular Biology. Washington, D.C., USA. May 16-20, 1998. American
Society for Biochemistry and Molecular Biology.
CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 12 Aug 1998
Last Updated on STN: 10 Sep 1998

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1997:643536 CAPLUS
DN 127:328199
TI New Inhibitors of Thrombin and Other Trypsin-like Proteases: Hydrogen
Bonding of an Aromatic Cyano Group with a Backbone Amide of the P1 Binding
Site Replaces Binding of a Basic Side Chain
AU Lee, Sheng-Lian; Alexander, Richard; Smallwood, Angela; Trievel, Raymond;
Mersinger, Lawrence; Weber, Patricia C.; Kettner, Charles
CS Chemical and Physical Sciences DuPont Experimental Station, DuPont Merck
Pharmaceutical Company, Wilmington, DE, 19880-0500, USA
SO Biochemistry (1997), 36(43), 13180-13186
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB Highly effective thrombin inhibitors have been obtained by preparing boronic
acid analogs of m-cyano-substituted phenylalanine and its incorporation

into peptides. The cyano group enhances binding by several orders of magnitude. For example, Ac-(D)Phe-Pro-boroPheOH binds to thrombin with a Ki of 320 nM and the Ki of Ac-(D)Phe-Pro-boroPhe(m-CN)-OH is 0.79 nM. Protein crystal structure determination of trypsin complexed to H-(D)Phe-Pro-boroPhe(m-CN)-OH indicates that the aromatic side chain is bound in the P1 binding site and that the cyano group can act as a H-bond acceptor for the amide proton of Gly219. Enhanced binding for inhibitors containing the m-cyano group was observed for coagulation factor Xa and for the factor VIIa·tissue factor complex [Ki values of Ac-(D)Phe-Pro-boroPhe(mCN)-OH are 760 and 3.3 nM, resp.]. This result is consistent with the sequence homol. of these two enzymes in the P1 binding site. Two enzymes lacking the strict homol. in the P1 binding site, pancreatic kallikrein and chymotrypsin, did not exhibit significantly enhanced binding.

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